REMARKS

Claims 3, 20-23, and 25-41 are active in the present application.

At the outset, Applicants wish to thank the Examiner for the indication that Claims 3 and 20-23 remain allowable (see paragraph 13 on page 12 of the Office Action dated August 7, 2006). Applicants also request withdrawal of the outstanding rejections in view of the amendments above.

The rejection of Claims 1, 4-19, and 24-41 under 35 U.S.C. §112, first paragraph (written description), is obviated in part by amendment and traversed in part.

The Examiner's criticisms of the claims as lacking sufficient written description appear to center on an allegation that the specification fails to disclose a genus of variants for the compounds of Formula (1) having inhibitory activity against MSH and their use as an active ingredient in a MSH inhibitory composition, a whitening agent, an immunofunction controlling agent, an appetite controlling agent, or cosmetic preparation (see page 3, lines 5-9 of the Office Action mailed December 22, 2005). The Examiner also alleges that the specification fails to describe how to identify an active amino acid, dipeptide or tripeptide compound within the scope of Formula (1).

Applicants remind the Examiner that MPEP § 2163.02 states:

> An objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." *In re Gostelli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989).

To this end, Applicants again direct the Examiner's attention to the painfully detailed description in the specification at pages 5 and 8-16 of the genus of variants for the

compounds of Formula (1). Applicants submit that the specification at pages 5 and 8-16 provides a more than adequate description to allow the skilled artisan to recognize what has been invented and what is claimed is adequately described in the specification within the meaning of 35 U.S.C. § 112, first paragraph. Further, it is believed that substantially all of the claimed genus would be functional for the intended purpose. In fact, contrary to the Examiner's allegations, it is readily apparent to the skilled artisan on the basis of this disclosure of how to determine and identify functional members of the claimed genus.

The further basis for this ground of criticism by the Examiner is that the examples presented in the present specification are not so broad as to embrace a diverse sampling of the claimed genus. However, the Examiner is reminded that the MPEP states in §2164.02:

> The specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation.

Therefore, the failure to recite and/or exemplify each any every possible diverse member of the claimed genus and explicitly demonstrate its operability within the claimed invention is of no matter. The question that should be asked is whether the scope of the claimed invention is described in accordance with the standard of *In re Gostelli.* Applicants submit that, indeed, the specification does.

To demonstrate the same, Applicants submitted a Declaration under 37 C.F.R. §1.132 executed by Dr. Eiji Shiojiri and Dr. Yoshinobu Takino ("the Shiojiri & Takino Declaration") on June 21, 2006. In the Shiojiri & Takino Declaration, a diverse spectrum of compounds within the scope of the originally claimed invention and the currently claimed invention were prepared. Subsequently, these compounds were assayed for melanocyte-stimulating hormone (MSH) inhibitory activity consistent with the description on pages 16-19 of the specification and the Test Examples. What is apparent from the Shiojiri & Takino Declaration is that the

skilled artisan can readily produce the compounds of the claimed invention and can readily identify and appreciate the active compounds, especially those that have inhibitory activity against MSH.

Moreover, Applicants direct the Examiner's attention to page 16, line 12 to page 19, line 2, which provides a full and detailed description of how to identify an *active* amino acid, dipeptide or tripeptide compound within the scope of Formula (1). Further, pages 19-24 describe how the skilled artisan would prepare compositions containing the compounds meeting the claimed activity limitation. And, still further, Applicants direct the Examiner's attention to the Shiojiri & Takino Declaration enclosed herewith that further illustrates the sufficiency of the present disclosure.

Moreover, Applicants direct the Examiner's attention to pages 25-43 in which Applicants have exemplified several synthetic methods to produce compounds of Formula (1) and methods by which the activity of the same may be ascertained. In particular, Applicants wish to now Test Examples 1, 2, and 4 by which the skilled artisan may readily identify functional compounds. Again, the Examiner is reminded of the standard for determining compliance with the written description requirement set forth in MPEP § 2163.02. In view of the foregoing, Applicants submit that in view of the extensive description in the specification the skilled artisan would be able to readily recognize that which they have invented and claimed.

Despite the foregoing, the Examiner has maintained this ground of rejection. In maintaining the written description rejection, the Examiner's major criticisms are that the claims lack sufficient written description because:

(a) substituents for $R^1 - R^4$ are undefined;

(b) the claims embrace an extremely large genus;

(c) only a handful of naphthyl-tripeptides have been provided in the specification as representative species; and

(d) no structure-function relationship has been disclosed so as to lead the artisan to believe that applicants were in possession of all the possible compounds within the scope of their claim that possess an ability to meet the claimed activity limitations.

In regard to criticism (a), Applicants submit that this criticism is moot in view of the removal of the substituted forms of the various moieties at positions R^1-R^4.

With respect to criticism (b), the Examiner is again reminded of the standard for determining compliance with the written description requirement set forth in MPEP § 2163.02. Further, the specification unequivocally *describes* the compounds of Formula (1) referring to the text at page 4, line 20 to page 6, line 17 and page 8, line 9 to page 14, line 18. The composition claims are described at page 19, line 3 to page 23, line 15. Therefore, the written description rejection over the compound and composition claims as presently written is improper and should be withdrawn.

In criticism (c), the Examiner again states that the rejection is based on the observation that the examples presented in the present specification are not so broad as to embrace a diverse sampling of the claimed genus. However, the Examiner is again reminded that the MPEP states in §2164.02:

> The specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation.

Therefore, the failure to recite and/or exemplify each any every possible diverse member of the claimed genus and explicitly demonstrate its operability within the claimed invention is of no matter. The question that should be asked is whether the scope of the

claimed invention is described in accordance with the standard of *In re Gostelli*. Applicants submit that, indeed, the specification does even if no working examples were given.

Nonetheless, to address criticisms (b) and (c), Applicants have amended the claims to limit the scope of the compound and composition claims to tripeptide derivatives of Formula (1). As the Examiner recognizes, several working examples have been provided for tripeptide derivatives of Formula (1) in the specification, as well as in the Shiojiri & Takino Declaration. Therefore, criticisms (b) and (c) should be withdrawn.

Criticism (d) can be found at lines 15-20 on page 6 of the Office Action mailed August 7, 2006, and appears to relate to the method of treatment claims. Although stated as a written description rejection, it appears that the Examiner has actually disguised an enablement rejection in the cloak of a written description rejection. However, in making this rejection the Examiner merely provides cursory conclusions that the skilled artisan would not be able to recognize that Applicants were in possession of the claimed invention in view of the extensive disclosure of the compounds of Formula (1), methods of making the same, compositions comprising the same, methods of administering the same, and the specific exemplified results set forth in the specification. Moreover, the Examiner makes no attempt to provide any reasons why the skilled artisan would be unable to recognize that Applicants were in possession of the claimed invention, nor any reason to doubt the objective truth of the statements contained in present specification related to the methods of treating presently claimed. Thus, the Examiner has failed to meet her burden in making out this rejection with respect to criticism (d). Further, Applicants direct the Examiner's attention to the discussion of the structure-function relationship below.

In view of the foregoing, Applicants submit that the skilled artisan would readily appreciate the scope of the claims as presently presented. As such, Applicants request withdrawal of this ground of rejection.

The rejection of Claims 8-10, 12-14, 16-18, 30-32, 34-36, and 38-40 (should be 39-40) under 35 U.S.C. §112, first paragraph (enablement), is obviated in part by amendment and traversed in part.

The Examiner has rejected the method of treatment claims (i.e., method of whitening, method of regulating immunofunction, and method of regulating appetite) as lacking enablement. The Examiner's primary criticism is that the specification merely discloses that the tested compounds have inhibitory activity against melanocyte-stimulating hormone (MSH), but does not exemplify the effectiveness of these tested compounds with respect to the various claimed methods. The Examiner further alleges that the specification "only discloses cursory conclusions without data supporting the findings" with respect to the methods of treatment.

To address this rejection Applicants: (a) have amended the claims to limit the inventive compounds to tripeptides (i.e., m=1), and (b) discussed several references correlating the demonstrated MSH inhibitory activity of the claimed compounds with efficacy in the various cited methods on pages 1-3 of the specification and **submit herewith** four references that establish that there is an art known correlation between MSH inhibition and efficacy in the various claimed methods.

With respect to point (a), the Examiner is reminded that several working examples have been provided for tripeptide derivatives of Formula (1) in the specification, as well as in

the Shiojiri & Takino Declaration. These working examples clearly establish the MSH inhibitory activity of the claimed compounds.

Turning to point (b), Applicants note that the paragraph bridging pages 2 and 3 and the first paragraph on page 3 cite many references that appear to address alternative (2). This paragraph and the references cited therein establish a link between MSH and skin pigmentation, thus supporting the method of whitening. Further, the references in the first paragraph on page 3 referred to as evidencing the known link between MSH and immunosupression and appetite control.

Moreover, to evidence the that correlation between MSH inhibition and the various methods of treatment are well known and, as such, no undue experimentation is necessary as the skilled artisan would readily appreciate the efficacy of these compounds once the MSH inhibition activity is established as in the present specification for the inventive compounds, Applicants **submit herewith**:

(i) Arbel-Malek et al. PNAS (1995), 92, 1789-1793, *which relates to whitening*;

(ii) Taylor et al. Neuroimmunomodulation (1994), 1, 188-194, *which relates to regulation of immunofunction*;

(iii) Hiltz et al. Cytokine (1992), 4(4), 320-328, *which relates to regulation of immunofunction*; and

(iv) Ludwig et al. Am. J. Physiol. Endocrinol. Metab. (1998), 274, E627-E633, *which relates to regulation of appetite*.

Applicants submit that they are the first to find the activities in the basic combination of a naphthyl group with a basic amino acid and neutral amion acid (Nal-(basic amino acid)-(neutral amino acid)). Those skilled in the art would easily be able to modify such a combination based on the description in the present specification, for example by introducing a substituent into the naphthyl group, esterifying the terminal carbonyl group, introducing an acyl group into the amino group, etc. These manipulations were well within the purview of

the skilled artisan at the time of the present invention and would require no undue experimentation. Further, with the established link between MSH inhibitory activity and the various pharmacological activities presently claimed, Applicants submit that the full scope of the presently claimed invention is sufficiently enabled as required by 35 U.S.C. §112, first paragraph.

In view of the foregoing, Applicants request withdrawal of this ground of rejection.

The rejection of Claims 24 and 25 under 35 U.S.C. §102(a) over Stewart et al is respectfully traversed on the grounds that this reference is not prior art against the present application.

The present application was filed on was filed on January 8, 2002, as a National Stage (371) of PCT/JP00/02687, filed on April 25, 2000, which claims priority to JP 11/118633, which was filed on April 26, 1999. Applicants note that the effective prior art date under 35 U.S.C. §102(e) for Stewart et al (WO 00/11022) is March 2, 2000. The effective prior art date for Stewart et al is over ten months after the filing date of the priority date of the present application of April 26, 1999. To perfect their claims to foreign priority to JP 11/118633, Applicants **submit herewith** certified English translation of JP 11/118633. Applicants request that the Examiner acknowledge entitlement of the present application to the benefit of an earlier filing date provided by the claim to priority to JP 11/118633, which is more than ten months prior to the effective filing date of Stewart et al. Since Stewart et al is not prior art against the present claims this ground of rejection should be withdrawn.

Applicants further note that Claims 24 and 25 have been amended to cancel "m = 0". The compounds cited by the Examiner in Stewart et al, each require "m" to be "0."

Therefore, Stewart et al does not anticipate the invention currently claimed in Claims 24 and 25.

In view of the foregoing, Applicants request withdrawal of the rejection over Stewart et al. Acknowledgment to this effect is requested.

The rejection of Claims 1, 4-19, and 24-41 under 35 U.S.C. §112, second paragraph, is obviated by amendment.

The Examiner's rejection is based on five apparent grounds of criticism:

1) the scope of substituents for R1, R2, R3, and/or R4;
2) the phrase "a unsubstituted aminoalkylene group having 1 to 6 carbon atoms and one or more substitutents" in Claims 1 and 24;
3) the use of the term "derivable from" in the phrase "an amino acid side-chain derivable from an amino acid having a hydrophobic side chain" in Claims 1 and 24;
4) the omission of essential steps in Claims 8-10, 12-14, 16-18, 30-32, 34-36, and 39-40; and
5) the identity of the object to be whitened.

In relation to criticisms (1) – (3) and part of (4), the claims have been amended to specifically address these criticisms. However, with respect to the "object" to be whitened, Applicants submit that the scope and meaning of the term "object" (criticism (5)) is sufficiently clear from the specification. In particular, the Examiner is referred to (for example) page 18, lines 17-22 and Test Example 2 in which the meaning of the "object" to be whitened can be readily understood. Therefore, no further amendment is believed to be necessary. Finally, with respect to criticism (4), Applicants note that the outcome for the treatment is inherent to the claimed method by virtue of contacting with the effective amount of the active compound. By the very meaning of the term "effective amount", the amount must be sufficient to effectively achieve the desired effect set forth in the preamble of the criticized claims. Therefore, no further amendment is believed to be necessary.

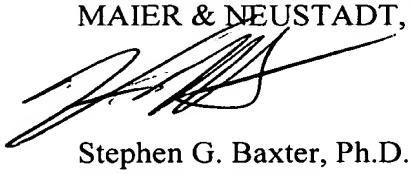
Withdrawal of this ground of rejection is requested.

Applicants submit that the present application is now in condition for allowance.

Early notification of such action is earnestly solicited.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.



Customer Number
22850

Tel: (703) 413-3000
Fax: (703) 413-2220
(OSMMN 08/03)

Stephen G. Baxter, Ph.D.
Attorney of Record
Registration No. 32,884

Vincent K. Shier, Ph.D.
Registration No. 50,552